REMARKS:

Status of Claims

Claims 38-39 and 41-61 are currently pending. Claims 38 and 39 have been amended. Support for the amendments are found throughout the specification as originally filed. Accordingly, Applicants submit that no new matter is introduced into the specification by way of the present amendments pursuant to 35 U.S.C. § 132. Applicants respectfully request entry of the amendments, reconsideration of the rejections, and allowance of the pending claims.

Claims 1-37, 40, and 62-67 are cancelled without prejudice or disclaimer as to the claimed subject matter. Applicants reserve the right to pursue canceled subject matter in one or more continuation or divisional applications, as appropriate.

Reply to Enablement Rejections Under 35 U.S.C. § 112, 1st Paragraph

Claims 38-44 are rejected for lack of enablement. Applicants respectfully disagree with this rejection. Nonetheless, claim 38, from which depend the remaining claims subject to the rejection, has been amended so that it is drawn to a method for treating a Chlamydia infection in a subject by administering to a subject in need thereof an effective amount of a therapeutic agent that disrupts the binding between cyclophilin A and a cyclophilin A binding partner. Applicants respectfully submit that this amendment obviates the rejection and its withdrawal is requested.

In order to establish a *prima facie* case of non-enablement, the examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure. See In re Wright, 999 F.2d 1557, 1561-562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). A disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, *unless* there is a reason to doubt the objective truth of the statements

contained therein which must be relied on for enabling support. See In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the court, it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Applicants again respectfully submit that the examiner has fail to meet this burden.

The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement. In re Morehouse, 545 F.2d 162, 165, 192 USPQ 29, 32 (CCPA 1976). Further, even a broad allegation that the disclosure is speculative, coupled with a recitation of various difficulties which might be encountered in practice, is not sufficient basis for requiring proof of operability. In re Chilowsky, 229 F.2d 457, 462, 108 USPQ 321, 325 (CCPA 1956). In the present case, Applicants respectfully submit that the examiner has not provided acceptable evidence that the claimed invention is inconsistent with enablement. At best, the examiner has made broad allegations that the disclosure is speculative and recited various difficulties which might be encountered in practice of the invention. This is not a sufficient evidentiary basis for requiring proof of enablement and a shifting of the burden of proof to appellant.

The examiner supports the rejection of lack of enablement with argument, but not with specific evidence. No specific evidence is presented that would doubt the objective truth of the current teaching that blocking the interaction between cyclophilin an its binding partners would effectively treat Chlamydia infection. In contrast, the specification provides data that demonstrate the ability of anti-cyclophilin A antibodies to block Chlamydia infection of human cells.

The examiner has presented several references that relate generally to the art of Chlamydia infection, which is purportedly set forth as evidence showing that the presently claimed methods are not enable by the present disclosure. Applicants respectfully submits that not one of the references cited by the Examiner provides any

evidence to refute the specific teachings of the current disclosure. The background teachings of the cited references provide an insufficient basis to "doubt the truth or accuracy of any statement in the supporting disclosure." M.P.E.P. § 2164.04. For example, Engel (Proc Natl Acad Sci U S A. 2004 Jul 6;101(27):9947-8) is relied upon by the examiner as evidence that "Chlamydia have a complex life cycle." See Office Action at page 7. Whereas the specific teachings of Engel may provide some general lessons to those of ordinary skill in the art, the reference in no way offers evidence that a person of ordinary skill in the art could not practice the method now claimed.

Schaechter *et al.* (Mechanisms of Microbial Diseases, Third Ed., 1999) is relied upon for the teaching that "'to be an effective treatment for a Chlamydia infection, an antimicrobial agent must penetrate four layers [of Chlamydia]". This teaching, however, is inapposite to whether a cyclophilin mechanism may be exploited to treat a Chlamydia infection. Nowhere in the specification is it suggested that, for example, a cyclophilin A antibody is used to kill the microorganism. Rather, the instant claims are directed to a method that exploits a mechanism that involves blocking the interaction between cyclophilin A and its binding partner. Thus, the analysis of whether or not an antimicrobial agent must penetrate four membrane layers to be effective is inapposite to the present invention.

Buzoni-Gatel *et al.* (Immunology. 1992 Oct;77(2):284-8.) is purportedly relied upon by the examiner for its teaching that "treatment with the anti-Lyt-2 in vivo and in vitro had no effect on the protection of Chlamydia." See Office Action at page 8, lines 7-8. Applicants fail to realized the relevance of this reference to the instant claims. Buzoni-Gatel *et al.* merely uses monoclonal antibodies as a research tool in an attempt to understand the role of Lyt-2+ T cells in conferring immunity. See Discussion at page 286, paragraph 3. The experiments disclosed in Buzoni-Gatel *et al.* are summarized in the abstract, which provides as follows:

> A murine model was used to study the respective roles of L3T4+ and Lyt-2+ T cells in protection against Chlamydia psittaci. Donor mice were intravenously (i.v.) infected with 1 x 10(5) plaque-forming units (PFU) per mice of live C. psittaci. One month after inoculation, splenic cells from donors were transferred into syngenic recipients (5 x 10(7) cells/mouse). As measured by splenic colonization on Day 6 after i.v. challenge (1 x 10(5) PFU/mouse), transfer with

primed (untreated) cells conferred a 3 log protection in this model. In vitro treatment, before transfer, of splenic cells with anti-Lyt-2 monoclonal antibody (mAb) and complement, markedly impaired the protection in comparison with control mice transferred with primed untreated cells, whereas treatment with anti-L3T4 mAb did not reduce the transferred protection. Resistance to a reinfection with C. psittaci was also studied after selective in vivo depletion of L3T4+ and Lyt-2+ T cells. One month after primary infection, mice were treated with anti-L3T4 or anti-Lyt-2 mAb and challenged thereafter (i.v., 1 x 10(5) PFU). The splenic colonization on Day 6 after challenge demonstrated that treatment with anti-Lyt-2 mAb impaired resistance against a subsequent infection with C. psittaci. Treatment with anti-L3T4 mAb in vivo had no effect on protection, as previously described in vitro. The mechanisms by which Lyt-2+ T cells could participate in the elimination of bacteria were discussed.

The antibodies described in Buzoni-Gatel *et al.* are differenct from the antibodies now disclosed; the mechanism studied in Buzoni-Gatel *et al.* is different from the mechanism now disclosed. Buzoni-Gatel *et al.* is clearly not relevant to the instant claims.

Longbottom (Vet J. 2006 Mar;171(2):263-75) is also relied upon by the examiner for its teaching of antibodies recognizing MOMP. See Office Action at page 8. Applicants again fail to realize the relevance of this reference to the instant claims. No specific evidence relevant to disrupting the binding between cyclophilin A and its binding partner can be found in this citation. Longbottom is also cited by the examiner for its teaching that "vaccination is the best approach for controlling the spread of chlamydia infections." See Office Action at page 9 (bottom). Applicants respectfully submit that this does not demonstrate that the currently claimed method is not enabled. Even assuming that this assertion if correct, the standard for enablement does not involve an analysis of whether or not the proposed invention is the best.

Zhang *et al.* (Infect Immun. 1989 Feb;57(2):636-8) is also relied upon by the examiner purportedly for its teaching of monoclonal antibodies exhibiting Chlamydia trachomatis serovar specificity (serovar A, B-Ba, or C) and serogroup specificity (B, intermediate, or C serogroup). See Office Action at page 8. Applicants again fail to realize the relevance of this reference to the instant claims. No specific evidence relevant to disrupting the binding between cyclophilin A and its binding partner can be found in this citation. This reference is clearly not relevant to the instant claims.

Lundemose *et al.* (Mol Microbiol. 1992 Sep;6(17):2539-48.) is relied upon by the examiner purportedly for its teaching that monoclonal and polyclonal antibodies raised against the recombinant Mip-like protein failed to demonstrate surface-exposed epitopes on infectious elementary bodies or reproductive reticulate body forms. See Office Action at pages 8-9. No specific evidence relevant to disrupting the binding between cyclophilin A and its binding partner can be found in this citation. Further, Mip-like protein is not the same as cyclophilin A, as is inferred by the examiner. See Office Action at page 9. Applicants again fail to realize the relevance of this reference to the instant claims.

Sherry *et al.* (Proc Natl Acad Sci U S A. 1998 Feb 17;95(4):1758-63) is relied upon by the examiner for allegedly supporting the premise that "the art questions if cyclophilin A is produced in response to a Chlamydia infection how can Chlamydia be treated by an antibody that is specific for cyclophilin A." This assertion, however, is factually unsupported. Sherry *et al.* is concerned with the role of cyclophilins in HIV-1 infection. The reference does not discuss Chlamydia and therefore can not support the examiner's premise. If anything, Sherry *et al.* lends credence to the operability of the recited method. Sherry *et al.* discloses the "our results indicate that agents targeting interaction between viral CyPA and surface-associated cellular CyPA-binding protein(s) reduce HIV-1 entry." See Sherry *et al.* at page 1762, second full paragraph.

Finally, the examiner relies on Greenspan *et al.* (Nat Biotechnol. 1999 Oct;17(10):936-7) for the premise that "defining epitopes is not as easy as it seems." See Office Action at page 9. Applicants again fail to realize the relevance of this reference to the instant claims. The claims are not directed to antibodies of particular epitopes. Further, difficulty is not determinative of nonenablement. No specific evidence relevant to present claims can be found in this reference.

Moreover, contrary to the examiner's contention, the specification provides guidance to one of ordinary skill in the art as to how to determine what therapeutic agents would be useful in the recited method without undue experimentation. The present inventors have discovered that the mechanism for Chalmydia infection may be mediated through a cyclophilin pathway. Indeed, Example 5 of the specification shows that

antibodies to cyclophilin blocks Chlamydia infection of human cells thereby demonstrating that disruption of cyclophilin mediated pathways is important to inhibiting Chlamydia infection. These results are not refuted by any specific evidence or reasonable rationale to the contrary. Thus, Applicants respectfully submit that the examiner has failed to establish a *prima facie* case of non-enablement

In view of the above, applicants request reconsideration and withdrawal of the rejection .

Applicants submit that the application is in condition for allowance. Please charge any fees due or credit any overpayment due to the undersigned's Deposit Account No. 50-0311, Reference No. 22058-536(AM101268).

Respectfully submitted,

42,267

David E. Johnson, Reg. No. 41,874
Sheridan K. Snedden, Reg. No. 55,998
Attorney/Agent for Applicants
c/o MINTZ, LEVIN
Tel: (617) 542-6000
Fax: (617) 542-2241
Customer No. 30623

Dated: January 28, 2007

4220684v.1